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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/763,210	01/26/2004	Noboru Yamaji	Q79353	6561

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EXAMINER	
CROWDER, CHUN	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 08/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/763,210	YAMAJI ET AL.	
	Examiner	Art Unit	
	Chun Crowder	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07/21/2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-17* is/are pending in the application.

4a) Of the above claim(s) *13-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 10/009,332.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The examiner of this application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Chun Crowder, Group Art Unit 1644, Technology Center 1600.

2. The instant application appears to be in sequence compliance for patent applications containing nucleotide sequence and/or amino acid sequence disclosures.

3. Applicant's election without traverse of Group I, claim 12, filed 07/21/2006, is acknowledged.

Claims 1-11 have been canceled.
Claims 12-17 are pending.

Claims 13-17 have been withdrawn from further consideration by the Examiner, under 37 C.F.R. § 1.142(b), as being drawn to nonelected inventions.

Claim 12 is under consideration in the instant application as it reads on an antibody against a metalloprotease of SEQ ID NO:1.

4. Applicant's claim for domestic priority is acknowledged. The priority applications 10/009,332 and PCT/JP00/07917 upon which benefit is claimed appear to provide adequate support under 35 U.S.C. 112 for subject matter claimed in the instant application.

If applicant desires to claim the benefit of a prior-filed application under 35 U.S.C. 121 and 365(c), a specific reference to the prior-filed application in compliance with 37 CFR 1.78(a) must be included in the first sentence(s) of the specification following the title or in an application data sheet. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph unless it appears in an application data sheet. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

The specification on page 1, line one should be amended to reflect the status of the priority applications 10/009,332, which are now US Patent 6,716,613, and to include a specific reference to the priority application PCT/JP00/07917 for which benefit is sought and the status of the instant application is a 371.

5. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

6. Applicant's IDS, filed 01/26/2004, is acknowledged and has been considered.

7. The disclosure is objected to because of the following informalities. The specification does not have the proper arrangement. The following order of arrangement is preferable in framing the specification.

Content of Specification

(a) Title of the Invention: See 37 CFR 1.72(a) and MPEP § 606. The title of the invention should be placed at the top of the first page of the specification unless the title is provided in an application data sheet. The title of the invention should be brief but technically accurate and descriptive, preferably from two to seven words may not contain more than 500 characters.

(b) Cross-References to Related Applications: See 37 CFR 1.78 and MPEP § 201.11.

(c) Statement Regarding Federally Sponsored Research and Development: See MPEP § 310.

(d) The Names Of The Parties To A Joint Research Agreement: See 37 CFR 1.71(g).

(e) Incorporation-By-Reference Of Material Submitted On a Compact Disc: The specification is required to include an incorporation-by-reference of electronic documents that are to become part of the permanent United States Patent and Trademark Office records in the file of a patent application. See 37 CFR 1.52(e) and MPEP § 608.05. Computer program listings (37 CFR 1.96(c)), "Sequence Listings" (37 CFR 1.821(c)), and tables having more than 50 pages of text were permitted as electronic documents on compact discs beginning on September 8, 2000.

Or alternatively, Reference to a "Microfiche Appendix": See MPEP § 608.05(a). "Microfiche Appendices" were accepted by the Office until March 1, 2001.

(f) Background of the Invention: See MPEP § 608.01(c). The specification should set forth the Background of the Invention in two parts:

(1) Field of the Invention: A statement of the field of art to which the invention pertains. This statement may include a paraphrasing of the applicable U.S. patent classification definitions of the subject matter of the claimed invention. This item may also be titled "Technical Field."

(2) Description of the Related Art including information disclosed under 37 CFR 1.97 and 37 CFR 1.98: A description of the related art known to the applicant and including, if applicable, references to specific related art and problems involved in the prior art which are solved by the applicant's invention. This item may also be titled "Background Art."

(g) Brief Summary of the Invention: See MPEP § 608.01(d). A brief summary or general statement of the invention as set forth in 37 CFR 1.73. The summary is separate and distinct from the abstract and is directed toward the invention rather than the disclosure as a whole. The summary may point out the advantages of the invention or how it solves problems previously existent in the prior art (and preferably indicated in the Background of the Invention). In chemical cases it should point out in general terms the utility of the invention. If possible, the nature and gist of the invention or the inventive concept should be set forth. Objects of the invention should be treated briefly and only to the extent that they contribute to an understanding of the invention.

(h) Brief Description of the Several Views of the Drawing(s): See MPEP § 608.01(f). A reference to and brief description of the drawing(s) as set forth in 37 CFR 1.74.

(i) Detailed Description of the Invention: See MPEP § 608.01(g). A description of the preferred embodiment(s) of the invention as required in 37 CFR 1.71. The description should be as short and specific as is necessary to describe the invention adequately and accurately. Where elements or groups of elements, compounds, and processes, which are conventional and generally widely known in the field of the invention described and their exact nature or type is not necessary for an understanding and use of the invention by a person skilled in the art, they should not be described in detail. However, where particularly complicated subject matter is involved or where the elements, compounds, or processes may not be commonly or widely known in the field, the specification should refer to another patent or readily available publication which adequately describes the subject matter.

(j) Claim or Claims: See 37 CFR 1.75 and MPEP § 608.01(m). The claim or claims must commence on separate sheet or electronic page (37 CFR 1.52(b)(3)). Where a claim sets forth a plurality of elements or steps, each element or step of the claim should be separated by a line indentation. There may be plural indentations to further segregate subcombinations or related steps. See 37 CFR 1.75 and MPEP § 608.01(i)-(p).

(k) Abstract of the Disclosure: See MPEP § 608.01(f). A brief narrative of the disclosure as a whole in a single paragraph of 150 words or less commencing on a separate sheet following the claims. In an international application which has entered the national stage (37 CFR 1.491(b)), the applicant need not submit an abstract commencing on a separate sheet if an abstract was published with the international application under PCT Article 21. The abstract that appears on the cover page of the pamphlet published by the International Bureau (IB) of the World Intellectual Property Organization (WIPO) is the abstract that will be used by the USPTO. See MPEP § 1893.03(e).

(l) Sequence Listing. See 37 CFR 1.821-1.825 and MPEP §§ 2421-2431. The requirement for a sequence listing applies to all sequences disclosed in a given application, whether the sequences are claimed or not. See MPEP § 2421.02.

In addition, the application is required to be reviewed and all spelling, TRADEMARK, and like errors corrected.

Trademarks should be capitalized or accompanied by the ™ or □ symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent application, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate correction is required.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12 is indefinite in the recitation of "represented by" (see claim 12, lines 3, 7, and 12) because the metes and bounds of the term is not clear and ambiguous. It is not clear what amino acid sequences are encompassed by "represented by" (e.g. open vs close languages) thus applicant fails to particularly point out and distinctly claim the subject matter which applicant regards as the invention. For examination purposes, "represented by" is interpretated as "comprising". See rejections below in Section 10.

Amending the claim to recite "consisting of" will obviate this rejection.

Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claim 12 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 12 recites "represented by", "1 to 10 amino acid residues are substituted, deleted, and/or inserted", and "90% or more sequence homology" as part of the invention.

The specification does not provide sufficient enabling description of the claimed invention. The specification discloses only protein with amino acid sequence of SEQ ID NO:1.

However, the term "represented by" in the claims are open-ended; it expands the sequence of SEQ ID NO:1 to include additional non-disclosed amino acid residues outside of the sequence shown in SEQ ID NO:1. Therefore, the instant claims encompass in their breadth any proteins comprising/having amino acid sequence disclosed in SEQ ID NO:1 and additional unknown amino acid residues.

Further, the disclosure appears to show only amino acid sequence of SEQ ID NO:1 (see pages 9-10 of the instant specification). The instant claim encompasses in its breadth *any* metalloprotease having aggrecanase activity wherein "1 to 10 amino acid residues are substituted, deleted, and/or inserted", and "90% or more sequence homology" of SEQ ID NO:1.

The art acknowledges that certain motifs of metalloproteases are critical for their aggrecanase activity. For example, Tortorella et al. (JBC 2000. 275;33:25791-25797) teach the thrombospondin type-1 (TSP-1) motif located within the C terminus of aggrecanase-1 is important for its enzymatic activity for cleavage of aggrecan; a truncated form of aggrecanase-1 lacking the TSP-1 motif is not able loses its aggrecanase activity (see entire document, particularly Figure 3 on page 25794).

Therefore, the skilled artisan would not know at the time the invention was made of all the contemplated amino acid sequence possibilities encompassed by the instant claims.

Furthermore, in addition to the lack of sufficient enabling description of the claimed genus of the metalloprotease that is "represented by", "1 to 10 amino acid residues are substituted, deleted, and/or inserted", and "90% or more sequence homology", applicant has not provided a sufficient enabling description of an antibody that selectively binds to such protein and/or variant protein, because such antibody would not reasonably be expected to be reactive with the polypeptide of SEQ ID NO:1, and therefore to be functional. For example, Lederman et al. (Molecular Immunology 1991. 28: 1171-1181. See entire document) disclose that a single amino acid substitution in a common allele ablates binding of a monoclonal antibody. Further, Li et al. (PNAS 1980. 77: 3211-3214. See entire document) disclose that dissociation of immunoreactivity from other biological activities when constructing analogs (see entire document).

Therefore, the specification does not provide for sufficient enablement for antibodies reactive with a metalloprotease "represented by", "1 to 10 amino acid residues are substituted, deleted, and/or inserted", and "90% or more sequence homology" of SEQ ID NO:1 other than those reactive with the polypeptide of SEQ ID NO:1.

In view of the lack of predictability of the art to which the invention pertains, working examples, the state of the art teachings, undue experimentation would be required to practice the claimed invention.

11. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

12. Claim 12 is rejected under 35 USC 101 because the claimed invention is directed to non-statutory subject matter.

Claim 12 is drawn to an antibody against a metalloprotease.

Claim 12, as written, does not sufficiently distinguish over antibodies as they exist naturally, e.g autoantibodies against a metalloprotease, because the claim does not particularly point out any non-naturally occurring differences between the claimed product and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980).

The claim should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified" as disclosed on pages 29-32 of the instant specification. See MPEP 2105.

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kuno et al. (JBC 1997. 272;1:556-562) in view of Campbell (Monoclonal Antibody Technology. 1984. Published by Elservier Science Publishers. Pages 1-32), Bost et al. (Immunol. Invest. 1988; 17:577-586) and Bendayan (J. Histochem. Cytochem. 1995; 43:881-886).

Kuno et al. isolated a metalloproteinase-disintegrin family protein with thrombospondin motifs (see entire document, particularly Materials and Methods on pages 556-557). The amino acid sequence from 249-633 of said metalloproteinase, containing metalloproteinase domain and the thrombospondin motif, is 63% identical to the amino acid of 213-583 of the claimed SEQ ID NO:1. Kuno et al. further taught that the isolated a metalloproteinase is up-regulated by inflammation mediators such as IL-1 and may play a role in cell proliferation, migration, and angiogenesis.

Kuno et al. differ from the claimed invention by not describing an antibody against a metalloproteinase.

However, methods making monoclonal antibody were well known in the art at the time the invention was made. For example, Campbell teaches methods of making monoclonal antibodies and the advantages of using antibodies in basic research, diagnostics and therapeutic uses (see entire document, particularly pages 2-23). Further, Campbell teaches that it is customary now for any group working on macromolecule to both clone the genes coding for it and make monoclonal antibodies to it, sometimes without a clear objective for their application (e.g. see page28).

Further, Bost et al. teach that antibodies can be specific and cross-react with the antigen. For example, antibodies which "cross-react" with IL-2 and HIV envelope protein, but establish that the binding of each protein is due to the presence of a homologous sequence in each protein in which 4 of 6 residues were identical (see entire document, but especially the Abstract and Discussion). Antibodies which bound either the HIV or IL-2 derived sequence did not cross-react with irrelevant peptides (e.g., "Results, page 579).

Furthermore, Bendayan teaches that the specific reactivity of a monoclonal antibody can be highly specific yet cross-react with antigens from different species or even distinct proteins not related to the original antigen (page 886, last paragraph).

Consequently, it was well known in the art at the time the invention was made that antibody binding of distinct proteins was indeed specific. Therefore, given the high degree of homology in amino acid sequence between the reference metalloproteinase and the claimed SEQ ID NO:1, the antibody made against the metalloproteinase taught by Kuno et al. would be specific to the claimed SEQ ID NO:1 in 213-582 region.

It would this have been obvious to the ordinary artisan at the time the invention was made to make an antibody to the claimed SEQ ID NO:1 in 213-582 region. The ordinary artisan would have been motivated to do so because it is customary for any group working on macromolecule to both clone the genes coding for it and make monoclonal antibodies for basic research, diagnostics and therapeutic uses and the claimed 213-582 region of SEQ ID NO:1 is highly homologous to the reference metalloproteinase that may play a role in cell proliferation, migration, and angiogenesis.

Given the teachings of Kuno et al. regarding the role of the isolated metalloproteinase, and the teachings of Campbell providing the method and advantages of making and using antibody, and Bost et al, and Bendayan regarding antibody cross-reactivity, the ordinary artisan at the time the invention was made would have had a reasonable expectation of success of producing the claimed antibody.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chun Crowder whose telephone number is (571) 272-8142. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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8/18/06

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August 16, 2006